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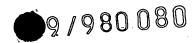
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(54) Title: 3-DIMENSIONAL IN VITRO MODELS OF MAMMALIAM TISSUES

(57) Abstract: Novel 3-dimensional in vitro models of mammalian tissues are provided. In a preferred embodiment, the models simulate behavior of human cancerous tissues at various stages of a solid tumour progression or the cell senescence, apoptosis or tissue regeneration in normal or cancerous human cells. The models are particularly useful for screening and testing of anticancerous drugs and assessing their toxicity for both the tumour and the surrounding tissue. Novel cellular automaton models for analysis and simulation of 3-dimensional cell organoids have also been developed. These models are useful for studying intercellular communication and predicting effects of gap junction channels modulating drugs.

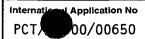


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(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 11006-98		of Transmittal of International Search Report (20) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/CA 00/00650	02/06/2000	03/06/1999
Applicant	· · · · · · · · · · · · · · · · · · ·	
NATIONAL RESEARCH COUNCIL	OF CANADA et al.	
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Aut ansmitted to the International Bureau.	nority and is transmitted to the applicant
This International Search Report consists It is also accompanied by	of a total of3 sheets. a copy of each prior art document cited in this	report.
Basis of the report		
With regard to the language, the language in which it was filed, unl	international search was carried out on the ba ess otherwise indicated under this item.	sis of the international application in the
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of t	he international application furnished to this
was carried out on the basis of the	d/or amino acid sequence disclosed in the ire sequence listing: nal application in written form.	sternational application, the international search
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the statement that the sub international application a	esequently furnished written sequence listing of sfiled has been furnished.	oes not go beyond the disclosure in the
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2. Certain claims were fou	nd unsearchable (See Box I).	
3. Unity of invention is lac	king (see Box II).	
4. With regard to the title ,		
X the text is approved as su	bmitted by the applicant.	
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5. With regard to the abstract , the text is approved as su the text has been establis within one month from the	bmitted by the applicant. hed, according to Rule 38.2(b), by this Authori date of mailing of this international search rep	ty as it appears in Box III. The applicant may, oort, submit comments to this Authority.
6. The figure of the drawings to be publ		
as suggested by the appli		X None of the figures.
because the applicant fail	ed to suggest a figure. characterizes the invention.	
L Decause this lighte better	onaracienzes the invention.	



A.	CLASS	IFICATION	OF SUB	JECT I	MATTER	
ΙP			15/00	•	C1201	/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) $IPC \ 7 \ C12N$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NYGAARD S J T ET AL: "Glioma cell invasion visualized by scanning confocal laser microscopy in an in vitro co-culture system." INVASION & METASTASIS, vol. 15, no. 5-6, 1995, pages 179-188, XP000971895 ISSN: 0251-1789 abstract	1-16,52
Υ	abstract	17-51
X	US 5 518 915 A (NAUGHTON ET AL.) 21 May 1996 (1996-05-21) claims 1-53	1
Y	 -/	17-36

Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
17 January 2001	05/02/2001
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk	Authorized officer
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Le Flao, K



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Internation Application No PCT 00/00650

		PCT 00/00650
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 314 805 A (HAUGLAND ET AL.) 24 May 1994 (1994-05-24) claims 1-20	37-51
Α	5141m3 1 20	14
X	NYGAARD SVEIN J T ET AL: "Dynamic determination of human glioma invasion in vitro." JOURNAL OF NEUROSURGERY, vol. 89, no. 3, 1998, pages 441-447, XP000971892 ISSN: 0022-3085 the whole document	1-16
X	FRESHNEY R I: "Culture of animal cells" 1987 , ALAN R. LISS , NEW YORK, US XP002157618 page 297 -page 307	1-17
A	DE RIDDER L: "Autologous confrontation of brain tumor derived spheroids with human dermal spheroids." ANTICANCER RESEARCH, vol. 17, no. 6B, November 1997 (1997-11), pages 4119-4120, XP000971885 ISSN: 0250-7005 the whole document	1-16
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i		·

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Information atent family members

Internation Application No
PCT/ 00/00650

D-11 :					
Patent document cited in search repor	t	Publication date	Patent fa member		Publication date
US 5518915	A	21 05 1006	UC FAA	12050 4	22 22 1005
02 2210312	A	21-05-1996		13950 A	22-08-1995
				6480 A	30-11-1993
				32508 A	16-07-1991
				3489 A	16-10-1990
			US 472	21096 A	26-01-1988
			US 596	52325 A	05-10-1999
			US 546	50939 A	24-10-1995
				10039 A	31-10-2000
				0254 A	23-04-1996
				2743 A	08-02-2000
				30781 A	03-12-1996
				16680 A	14-05-1996
				2475 A	30-04-1996
				11107 A	30-07-1996
				.6681 A	14-05-1996
				8485 A	26-11-1996
				85964 A	28-07-1998
				24840 A	29-04-1997
			US 590	2741 A	11-05-1999
			US 586	3531 A	26-01-1999
			US 584	19588 A	15-12-1998
				8721 A	12-01-1999
				4578 B	16-12-1993
				1489 A	02-04-1990
				7642 A	20-08-1991
				35657 A	23-05-1995
				0591 A	07-05-1991
				8506 A	14-03-1990
				6393 A	28-08-1991
				1536 A	31-10-1996
				9158 A	11-07-2000
				1657 T	26-03-1992
				6571 B	15-10-1998
				6684 B	15-10-1998
				6685 B	15-10-1998
				.0787 A	22-04-1991
			NZ 23	80572 A	23-12-1993
				1676 A	30-03-1990
				2796 A	22-03-1990
				0490 A	03-11-1992
				6886 A	27-06-1990
				7692 T	15-09-1995
				.5990 A	14-03-1991
				.6090 A	14-03-1991
				.5414 B	03-10-1991
				6887 A	09-11-1987
				1337 A	15-04-1993
				7673 A	15-08-1989
			CA 131	.0926 A	01-12-1992
US 5314805	Α	24-05-1994	NONE		